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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/595,096	06/15/2000	David J. Diller	1073.060	8927

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EXAMINER	
MORAN, MARJORIE A	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 06/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/595,096	DILLER ET AL.	
	Examiner	Art Unit	
	Marjorie A. Moran	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/17/04 has been entered. Claims 1-30 are pending.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a NEW MATTER rejection.

A method, system and program (on a computer-readable storage device) for modaling ligand-protein complexes "so as to identify ligands likely to have a therapeutic activity", as recited in the amended claims, is new matter. The original claims were directed to a method and devices for docking a ligand into a protein, and did not recite any intended use with regard to "identification" of either the ligand or protein. The originally filed specification teaches on page 3 that the "ultimate goal" of the invention is to use molecular docking as a way to prioritize combinatorial library screening efforts, but does not disclose anywhere what the screening is to

be prioritized *for*. It is noted that it is generally known in the art that combinatorial libraries may be screened for a variety of activities, including those NOT related to "therapeutic purposes"'; e.g. screening for better catalysts or co-catalysts for use in inorganic reactions. Page 25 of the originally field specification teaches that one "problem" solved by the instant invention is ranking of docked compounds. However, the specification does not teach what activity, if any, is related to the "ranking". Further, the specification does not disclose whether "fitting" or docking of a compound into a site implies any therapeutic activity at all. The specification exemplifies, on pages 27-28, docking of different conformations of an HIV protease inhibitor into a binding site (presumably of HIV protease?), but does not disclose that this is an example of *identification* of a ligand, nor whether any particular conformation would be expected to "have therapeutic activity". Applicant states in the response filed 2/17/4 that the amendment finds "support in the specification as filed", but does not point to explicit support; e.g. by page and line number. As support for a method, system, or program for identifying ligands "likely to have therapeutic activity" is not found in the originally filed specification or claims, the claims recite new matter and are rejected.

Claims 1-30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This is a LACK OF ENABLEMENT rejection.

The factors to be considered in determining what constitutes undue experimentation were affirmed by the court in *In re Wands* (8 USPQ2d 1400 (CAFC 1986)). These factors are the quantity of experimentation; the amount of direction or guidance presented in the specification; the presence or absence of working examples; the nature of the invention; the state of the prior art; the level of skill of those in the art; predictability or unpredictability of the art; and the breadth of the claims.

As set forth above, the specification fails to provide support for a method, system of program for identifying ligands "likely to have therapeutic activity" using the claimed method/program steps. The steps recited are directed to optimizing docking or fitting of a ligand into a binding site. It is noted that the mere fact that a compound "fits" or may dock into a binding site of a protein does not imply anything about the activity of the compound. For example, it is generally known in the prior art that water molecules and ions may "dock" into a binding site of a protein (e.g. modeling and calculation of solvation is well-known in the prior art), but fail to have any particular therapeutic activity. No steps of comparison to compounds with known therapeutic activity, such that therapeutic activity of an "unknown compound" may be imputed, are recited in the claims. The intended use newly recited in the claims is quite broad. A compound may be as likely to have positive as negative "therapeutic" activity upon binding to a protein; the claims do not distinguish between positive and negative therapeutic activity and do not recite any steps of differentiation. For example, both activators and inhibitors may bind to the same site of a protein or enzyme. Mere knowledge that a compound binds to a site does not necessarily identify the compound as having therapeutic activity. One must have some knowledge of whether greater or less activity of the protein is desired in order to identify a compound with the appropriate activity, then must have some way to determine whether a compound actually HAS the desired effect. As set forth above, the instant specification does provide working examples of fitting or docking different conformations of an HIV protease inhibitor into a binding site, on pages 27-28, but does not disclose anywhere how to identify any of the conformations as having (or likely to have) therapeutic activity. For example, if a particular conformation binds more tightly, might it act as an HIV protease activator or agonist? Absent any step of confirming activity, or comparison to a compound with known activity and attributes (e.g. it is known that binding more tightly is likely to cause greater inhibition), one

skilled in the art would not know how to determine whether a compound has therapeutic activity merely by optimizing the position of a ligand in a binding site of a protein. The level of one of skill in the "computer simulation" art is acknowledged to be high. However, for the reasons set forth above, it would require undue experimentation by one skilled in the art to identify a ligand likely to have therapeutic activity using only the claimed method steps, therefore the claims are not enabled.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-20 are again rejected, as previously set forth in the office actions of 5/16/03 and 12/17/03, under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Applicant's arguments filed 2/17/04 have been fully considered but they are not persuasive. In response to applicant's arguments that all the claims recite a concrete, tangible and useful result and are therefore statutory, applicant is reminded that the claims are directed to different categories of invention. A process (method) limited to be implemented by a computer may be subject to this analysis. However, claims directed to a physical device or apparatus (e.g. a computer-readable medium) are necessarily statutory. This distinction is reflected in the rejection set forth above. Claims 21-30, clearly directed to a *device* (i.e. product), are statutory, and are not rejected herein.

With regard to the "computer-aided system" of claims 11-20, it is again noted that the claims directed to the system do not recite any structural or physical limitations such that it is

clear that the "system" is intended to be a device and not just a series of instructions to a computer. It is further noted that that claims do not actually recite a "computer".

As set forth in MPEP 2106.IV.B.1(a): "computer programs claimed as computer listings per se, i.e., the descriptions or expressions of the programs, are not physical "things." They are neither computer components nor statutory processes, as they are not "acts" being performed. Such claimed computer programs do not define any structural and functional interrelationships between the computer program and other claimed elements of a computer which permit the computer program's functionality to be realized. In contrast, a claimed computer-readable medium encoded with a computer program is a computer element which defines structural and functional interrelationships between the computer program and the rest of the computer which permit the computer program's functionality to be realized, and is thus statutory. Accordingly, it is important to distinguish claims that define descriptive material per se from claims that define statutory inventions.

Computer programs are often recited as part of a claim. Office personnel should determine whether the computer program is being claimed as part of an otherwise statutory manufacture or machine. In such a case, the claim remains statutory irrespective of the fact that a computer program is included in the claim. The same result occurs when a computer program is used in a computerized process where the computer executes the instructions set forth in the computer program. Only when the claimed invention taken as a whole is directed to a mere program listing, i.e., to only its description or expression, is it descriptive material per se and hence nonstatutory.

Since a computer program is merely a set of instructions capable of being executed by a computer, the computer program itself is not a process and Office personnel should treat a claim for a computer program, without the computer-readable medium needed to realize the computer program's functionality, as nonstatutory functional descriptive material. When a computer program is claimed in a process where the computer is executing the computer program's instructions, Office personnel should treat the claim as a process claim. See paragraph IV.B.2(b), below. When a computer program is recited in conjunction with a physical structure, such as a computer memory, Office personnel should treat the claim as a product claim. See paragraph IV.B.2(a), below."

The fact that the program intended to be implemented by the system of claims 11-20 is "the same" as the program embodied on the program storage device of claims 21-30 does not affect the category of invention or the statutory status of the claims reciting the program. To further clarify, claims 21-30 are clearly direcetd to a device, or product, and are thus statutory. Claims 11-20 are directed to a "system" comprising a program. No physical or "hardware" limitations are recited in claims 11-20, therefore it does not appear that the claimed "system" is a physical product, but is merely a listing of computer-implemented steps; i.e. a computer program. *A computer program, per se, is not statutory subject matter.*

Claims 1-10 are directed to a computer-implemented method. Such a method MAY be statutory is it recites a "safe harbor"; e.g. a physical act outside the computer. For a definition and further examples of "safe harbors", see MPEP 2106. As noted by applicant in the response, and in the ATT decision, a computer-implemented method need not necessarily recite a physical step. A computer-implemented method MAY also be statutory where it recites a concrete, tangible and useful result. Applicant apparently agrees, as evidenced by the argument set forth on page 12 of the response, and argues that the concrete, tangible and

useful product of the claims is "a model of a ligand-protein complex that is indicative of whether the ligand will have therapeutic activity".

In response, it is noted that the claims fail to recite any actual steps for identifying a ligand "likely to have therapeutic activity". In fact, no identification step of any kind is recited in the claims. The only steps recited are those of optimizing the position of a ligand in relation to a protein. As set forth above, simply "fitting" a ligand into a protein, whether such fitting is "optimized" or not, does not indicate anything about the possible therapeutic activity of the ligand. As the claimed method does not actually result in identification of a ligand "likely to have therapeutic activity", the results of the claimed docking method do not provide a concrete, tangible and useful result, therefore the examiner maintains that the claims are not statutory, and the rejection is maintained.

Claims 1-30 are again rejected, as set forth in previous office actions, under 35 U.S.C. 101 because the claimed invention lacks patentable utility.

Applicant's arguments filed 2/17/04 have been fully considered but they are not persuasive. The claims are directed to a method, and a "system" and program for performing the method, for identifying a ligand "likely to have therapeutic activity". As set forth above, the claims do not recite any steps of actually identifying a ligand with such activity, and the specification does not provide support for the claimed method, thus neither the specification nor claims provide support for the utility argued in the response of 2/17/04. The fact that the claimed method "can be commercialized" does not impute utility to the claimed invention. For the reasons set forth above, and those previously set forth, the examiner maintains the rejection.

Conclusion

Claims 1-30 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marjorie A. Moran whose telephone number is (571) 272-0720. The examiner can normally be reached on Mon. to Wed, 7:30-4; Thurs 7:30-6; Fri 7-1 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571)272-0722. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Marjorie A. Moran
Primary Examiner
Art Unit 1631

mam

Marjorie A. Moran
6/1/04